

*REMARKS/ARGUMENTS**The Pending Claims*

Claims 1-4, 6, and 9-14 are pending and are directed to a library of membrane protein-embedded liposomes (claims 9-11 and 14) and a method of preparing the library (claims 1-4, 6, 12, and 13).

Claims 1-4, 6, 12, and 13 have been labeled as withdrawn, because these claims are directed to a non-elected invention in response to the earlier restriction requirement. Since claims 1-4, 6, 12, and 13 depend from the elected claims and are directed to a method of preparing the library of the elected claims, Applicants request that claims 1-4, 6, 12, and 13 be rejoined and considered upon the allowance of claims directed to the elected subject matter.

*Amendments to the Claims*

Claim 8 has been canceled, and claims 1, 9, and 11 (which previously depended from claim 8) have been amended to depend from claim 14. Claim 14 has been amended to recite that the liposomes have a diameter of 10-5000 nm as supported by the specification at, for example, page 21, lines 9-10, and page 22, lines 6-7.

Accordingly, no new matter has been added by way of these amendments to the claims.

*Summary of the Office Action*

The Office maintains the rejection of claims 8-11 and newly rejects claim 14 under 35 U.S.C. § 103(a) as allegedly unpatentable over Allen et al. (U.S. Patent 6,056,973) and Tanaka et al. (WO 02/056026). The Office also maintains the rejection of claims 8-11 and newly rejects claims 14 under 35 U.S.C. § 103(a) as allegedly unpatentable over Perrott et al. (U.S. Patent 6,217,901), Tanaka et al., and Munechika et al. (U.S. Patent 5,662,931).

Reconsideration of these rejections is hereby requested.

*Discussion of the Obviousness Rejections*

The Office contends that it would have been obvious to one of ordinary skill in the art to make the library of membrane protein-embedded liposomes recited in claims 8-11 and 14 based on the teachings of (i) the Allen and Tanaka references and (ii) the Perrott, Tanaka, and Munechika references. The obviousness rejections are traversed for the following reasons.

*A. Tanaka et al. is not prior art to the subject matter of the pending claims*

In response to Applicants' previous arguments to remove Tanaka et al. as prior art, the Office contends that U.S. Patent Application 10/622,002 (to which the current application claims priority) does not have support for the open-ended range of 10 nm or more of the diameter of the liposomes, as previously recited in claim 14.

Claim 14, as amended, recites a library of membrane protein-embedded liposomes comprising about  $1 \times 10^6$  or more membrane protein-embedded liposomes, which library of membrane protein-embedded liposomes is obtained by (a) providing a library of membrane proteins, and (b) contacting the library of membrane proteins with liposomes to form a library of membrane protein-embedded liposomes, wherein the weight ratio of the membrane proteins to lipids constituting the liposomes is 0.05 or less, *wherein the liposomes have a diameter of 10-5000 nm*, and wherein the amount of membrane proteins per library is about 10 fg or more. Claim 8 has been canceled, and the remaining claims have been amended to depend from claim 14.

U.S. Patent Application 10/622,002 recites liposome diameter ranges of 10 nm to 5000 nm (see, e.g., page 24, lines 25-30). Therefore, the subject matter of claim 14 and the claims dependent thereon is entitled to the benefit of the filing date of U.S. Patent Application 10/622,002. Accordingly, the pending claims have an effective U.S. filing date of July 17, 2003.

Tanaka et al. has an earliest possible effective U.S. filing date of January 9, 2001, and was published on July 18, 2002, i.e., within one year of the priority date of the pending claims of July 17, 2003. As a result, Tanaka et al. can only possibly be prior art to the pending claims under Section 102(a) or Section 102(e).

Applicants believe that the Declaration Under 37 C.F.R. § 1.132 submitted with the previous Reply to Office Action is sufficient to demonstrate that Tanaka et al. is not prior art to the pending claims under Section 102(a). Additionally, Applicants believe that the evidence of common ownership between the subject matter of the Tanaka et al. and the claimed invention of the pending application at the time that the invention was made set forth in the previous Reply to Office Action is sufficient to demonstrate that Tanaka et al. is not prior art to the pending claims under Section 102(e). Accordingly, Tanaka et al. cannot be relied upon as prior art under Section 102(a) or 102(e) against the pending claims for purposes of determining obviousness under Section 103(a).

*B. The remaining references do not render obvious the claimed subject matter*

For the reasons set forth in the previous Reply to Office Action, the remaining cited references, when considered alone or in combination, do not render obvious the claimed subject matter. In particular, none of the cited references, when considered alone or in combination, discloses a library of membrane protein-embedded liposomes with the claimed properties (e.g., the particular weight ratio of membrane protein/lipid). As set forth in the specification, the number of membrane proteins embedded per liposome, the size of the liposome, and the like (e.g., weight ratio of membrane protein/lipid) influence the properties of the library used for the proteome analysis of membrane proteins (see, e.g., page 8, lines 2-16).

The Office contends that Allen et al. discloses a liposome formation with 1-20 mole percent of lipid and 1.2 mole percent of protein. Since the molecular weight of lipid constituting a liposome is about 800, and the average molecular weight of membrane proteins typically is several tens of thousands of Daltons (Da), e.g., 30 kDa, the weight ratio of membrane protein/lipid would be on the order of about 2 to about 40 or more. In distinct contrast, the particular weight ratio of membrane protein/lipid set forth in the pending claims is 0.05 or less, i.e., far less than the weight ratio of membrane protein/lipid possibly disclosed in Allen et al.

If anything, the disclosure of Allen et al. teaches away from using the weight ratio of membrane protein/lipid of 0.05 or less, as recited in the pending claims. Therefore, it would

not have been obvious to one of ordinary skill in the art to use a weight ratio of membrane protein/lipid of 0.05 or less based on the disclosure of Allen et al.

The Office acknowledges that Perrott et al. does not teach a weight ratio of membrane protein/lipid that falls within the claimed range; however, the Office contends that Munechika et al. teaches a weight ratio of protein/lipid of 0.1 to 0.5. Applicants note that Munechika et al. relates to a liposome composition *encapsulating* a protein drug. The proteins exemplified in Munechika et al. are *water-soluble* proteins, such as cytokines and hormones. As such, one of ordinary skill in the art would not have had any reason to combine the disclosure of Munechika et al. with the disclosure of Perrott et al., let alone in the manner necessary to arrive at the inventive library, wherein *membrane* proteins are embedded into the lipid bilayer of the proteoliposome.

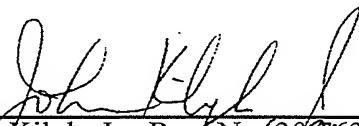
Furthermore, Applicants note that each of the Allen, Perrott, and Munechika references merely discloses liposomes containing only one kind of therapeutic or target protein. In contrast, the inventive library of membrane protein-embedded liposomes and methods of the library can be used to analyze all the membrane proteins in the body, wherein the native structure and function of each protein constituting the library is maintained (see, e.g., page 7, line 15, through page 8, line 21, of the specification).

For the above-described reasons, it would not have been obvious to one of ordinary skill in the art at the relevant time to arrive at the present invention in view of the Allen, Perrott, and Munechika references. Accordingly, the obviousness rejections should be withdrawn.

*Conclusion*

Applicants respectfully submit that the patent application is in condition for allowance. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,



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